# BIOSENSORS: Microelectronics Marries Biology

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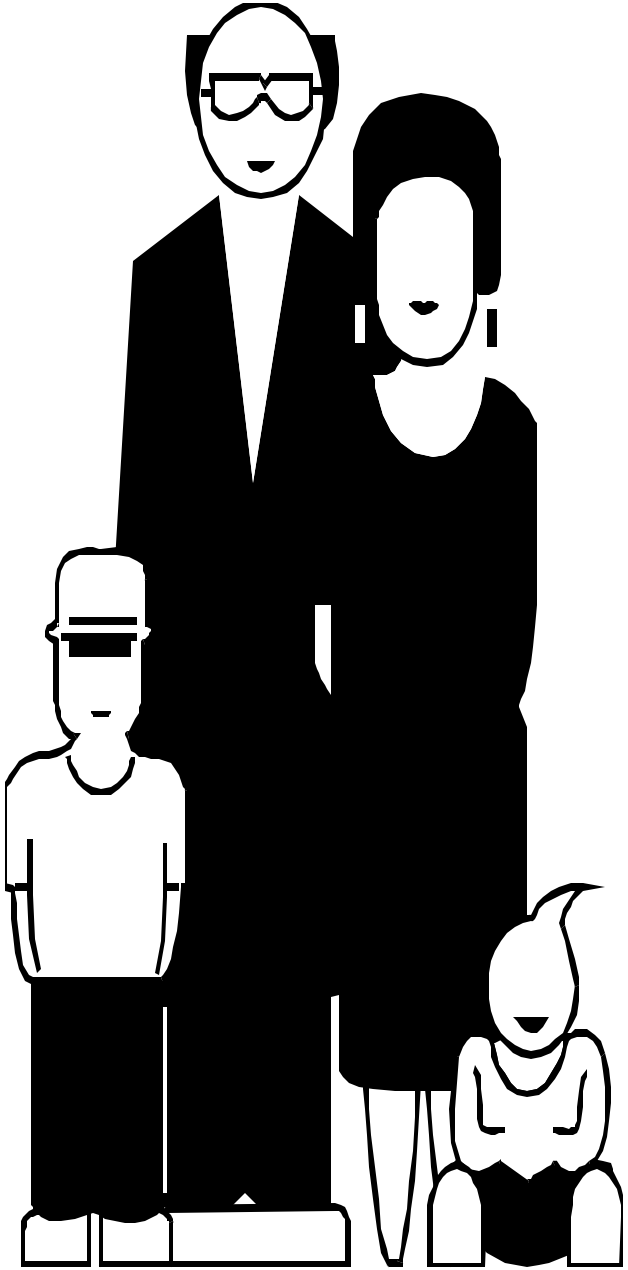

# Biosensors

- What is a Biosensor
- The Past (History)
- The Present
- Issues Unique to...
- Biosensors and their applications
- Challenges to Success
- The Future

# What is a Biosensor?

Electronic device

> uses biological elements--antibodies, enzymes, cells--as the analyte sensor;

>Couples the element to a transducer

- Biological molecule with the power of modern electronics
- Sophisticated descendant of the canary in the coal mine

# The Past

- Evolution began in the mid-1950's
- Invention of an electrode to measure dissolved oxygen in the blood
- By 1962, extended "oxygen electrode" to sense blood glucose levels
- Blood glucose monitoring kits - successful commercial Biosensors

# The Present

- Most common Biosensors are enzyme or antibody based
- Many companies developing DNA-based biochip arrays
- Researchers working to affix entire living cells to a chip

# Unique Issues

- Testing Context
- Operator gives direct patient care
- Monitoring, rather than diagnosis
- Stability may be more important than accuracy
- Testing over limited time frame

# Unique Issues (cont.....)

- Testing does not involve separable specimen
- Method validation/verification difficult or impossible
- Calibration verification difficult or impossible

# Unique Issues (cont.....)

- QC usually limited to comparison with specimens from the same patient tested in laboratory
- Proficiency testing usually impossible

# Unique Issues (cont.....)

- Inflexibility
- Calibration is frequently factory-set or performed only once before testing is begun
- Adverse testing conditions
- Bio-compatibility issues: thrombus formation or immune response

# Invasive & Minimally-Invasive Testing

- Extra-corporeal sensor
  - In-line testing
  - Shunted outside
    - either returned to circulation or discarded

# Invasive & Minimally-Invasive Testing (cont.....)

- Invasive sampling/external sensor

  --Ex vivo sensors

  --Arterial or venous specimen is shunted outside, tested and returned

# Invasive & Minimally-Invasive Testing (cont.....)

- In vivo sensors

  --continuous monitoring with indwelling sensors

  --intravenous, intra-arterial or intra-peritoneal

# Extra-Corporeal Circuits

- Analytes: $SpO_2$, hematocrit, and change in blood volume
- Methodology:  During dialysis, light is passed through the chamber to detect change in $O_2$ saturation. Hematocrit is derived from light scatter and absorption
- Calibration:  Factory calibration
- Quality Control:  “Verification filter” with specified tolerance
- Lifetime:  Disposable after dialysis

# Extra-Corporeal Circuits

- Analytes: pH, pC02, p02,K+, temperature, S02, Hct, Hgb
- Methodology:  Continuous Intra-arterial testing.  On demand, blood is shunted into contact with 4 optodes.
- Calibration:  Tonometered calibration at the bedside.
- Quality Control:  Simultaneous lab test
- Lifetime: Disposable after surgery

# Ex Vivo

- Analytes: pH, pC02, p02,. Bicarb, BE, Sa02, and TCO2
- Methodology:  Specimen is aspirated into sensor, tested & returned to circulation.
- Calibration:  2-level calibration using standards introduced by an independent Luer lock stopcock.
- Quality Control:  Amid-level calibration  using standards introduced after the device is attached to the patient
- Lifetime:  144 hours or 200 measurements

# Ex Vivo

- Analytes: pH, pC02, p02, Hct, Na+, K+, bicarb, BE, TCO2
- Methodology:  Specimen is withdrawn, tested & returned to circulation.
- Calibration:  Initially a 2-level calibration; one-point calibrations can be done before each test
- Quality Control:  Simultaneous test
- Lifetime 72 hours

# In Vivo

- Analytes: pH, pC02, and temperature
- Methodology:  Indwelling arterial sensors that provides continuous monitoring using 3 separate optodes for fluorescent detection
- Calibration: 3 levels of Tonometered solution are used to calibrate just before insertion.
- Quality Control:  None besides simultaneous lab test

# Challenges to Success

- Obstacles to reliable in vivo testing have not yet been overcome
- Biomolecules used for recognition are not stable or robust
- The trend toward miniaturization and full automation demand more advances

# The Future

- Changing Boundaries and Definitions
- Evolving Standards and Regulations